Chapter 4
Brain-Computer Interfaces and Therapy

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4.1 Introduction

Brain–computer interfaces (BCIs) have historically primarily been developed to provide alternative communication devices to people disabled by neuromuscular disorders such as amyotrophic lateral sclerosis, cerebral palsy, stroke, or spinal cord injury. BCIs acquire brain signals, analyze them, and translate them into commands that are relayed to output devices that carry out desired actions (Shih et al. 2012). Only recently has the idea been advanced that BCI technology can be used not to extract brain activity to control the external environment but in the opposite direction toward the brain to control brain mechanisms to improve functions and sustain recovery (Grosse-Wentrup et al. 2011; Rossini et al. 2012). This change in BCI research and application raises ethical issues quite different from those previously addressed (Tamburrini 2009; Clausen 2011; Shih et al. 2012; Schneider et al. 2013). Previous interest in ethical BCI arguments focused on BCI technology as a means to provide an alternative channel of communication to disabled people and eventually to healthy people in specific contexts. Much less attention has been given to therapeutic application. Here we would like to focus on ethical, social, and cultural aspects that might stem from the application of BCI technology to treat brain lesions specifically favoring functional recovery.

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4.2 BCI, Neurofeedback and EEG-Based Treatment Protocols

Electromagnetic brain signals have been extensively studied and a large body of evidence indicates the capacity of EEG analyses to detect brain activity related to specific functions and its physiological or pathological changes. Even more challenging and interesting as a potential therapeutic tool is the possibility of volitional modulation of brain activity. In this latter field data are scarce but promising findings have been reported on the capacity by volitional modulation of slow cortical potentials of reducing seizure frequency (Rockstroh et al. 1993) and to improve ADHD symptoms (Strehl et al. 2006). Recently different groups have addressed the possibility of improving stroke rehabilitation through BCI or neural-brain-computer interface (NBCI) derived approaches (Grosse-Wentrup et al. 2011; Bundy et al. 2012; Pichiorri et al. 2012). In these approaches it is not clear whether we are facing a BCI application or innovative neurofeedback protocols. On the other hand, as recently pointed out (Allison 2011), much confusion still exists in defining BCI. Literally one would refer to BCI when brain activity is used to control an external device even if the device is used to provide therapy, for instance using BCI for controlling attention during gait robotic training (Broetz et al. 2010). On the other hand neurofeedback would imply providing a subject with information of ongoing brain activity in order to voluntarily modulate it (de Zambotti et al. 2012). A third condition, somehow in between, is that in which the subject is not directly aware of the characteristic of the ongoing brain activity but the performance of an external device is used to guide the modulation of the recorded brain (Mattia et al. 2013). In all three conditions the basic idea is to drive brain activity toward a recovery/improvement of the damaged function. To achieve this a somehow automatic close link is instated so as to favor the rearrangement of brain synapses and circuits considered the substrate of functional recovery (Nudo 2007). Despite differences in definition, as regards ethical issues the three approaches are largely similar. In the following we will address different clinical conditions focusing on non-technical aspects related to BCI and related technology-based therapies.

4.3 BCI and Rehabilitation of Motor Functions

Among the possible applications of BCI technology, the neurorehabilitation of motor function in stroke survivors is constantly gaining interest among researchers and is gathering a considerable amount of resources in the field. In recent years the application of BCI in stroke rehabilitation has been investigated by different groups, either with preliminary studies on healthy subjects (Nagaoka et al. 2010; Gomez-Rodrig 2011) or with case reports (Daly et al. 2009; Broetz et al. 2010) and small clinical trials (Buch et al. 2008; Prasad et al. 2010).

The theoretical framework to support such interventions regards BCI systems (either alone or combined with neuroprosthetic devices) capable of enhancing activity-dependent neuroplasticity (Nudo 2007) guiding the spontaneous plastic changes occurring in the brain after stroke towards a more normal brain activity that in the end would mean a better recovery outcome.

Two different strategies have been identified: the first strategy foresees the use of BCIs to train patients to produce more normal brain activity; the hypothesis behind this approach is that more normal brain activity reflects more normal brain function, and more normal brain function results in an improvement of motor control. The second strategy is to use BCIs to operate devices which are capable of assisting movement: The sensory input resulting from this assisted movement induces plastic changes in the central nervous system leading to better motor function (Daly and Wolpaw 2008). The latter approach was explored in the first trial involving stroke patients in a BCI paradigm for motor rehabilitative purposes (Buch et al. 2008). In this study, patients with no residual finger function underwent a motor imagery MEG-based BCI training in order to operate a mechanical orthosis that passively flexed or extended their fingers. Similar approaches have been used in other studies, albeit mainly based on EEG signals (Broetz et al. 2010; Ang et al. 2010; Dimyan and Cohen 2011; Caria et al. 2011). Of particular interest are the differences in the methods used to select the features of the brain activity to be strengthened by the rehab protocol. In the first MEG study (Buch et al. 2008) the features chosen were those that best discriminated the motor imagery from the rest condition regardless of their location on the scalp (either collected from the lesioned hemisphere or the intact one). In the other cited studies control features selection was guided by the idea that for motor recovery application, the source of the signal adopted for BCI training must be as close as possible to normal activity. Thus, features were selected comparing the EEG activity generated from motor imagery (MI) of the affected hand to that generated from MI of the unaffected one (Daly et al. 2009), or the control signal was collected from the ipsilesional hemisphere only (contralateral to the imagined movement of the affected hand) (Broetz et al. 2010; Ang et al. 2010; Caria et al. 2011). Why is the method chosen to select control features relevant? Sensorimotor rhythm-based BCI training has long-lasting effects on brain plasticity (Ros et al. 2010; Pichiorri et al. 2011) and it is conceivable that different sensorimotor rhythms are sustained by different circuits. If this is the case differences in the brain rhythm used in the BCI application would imply differences in the therapeutic effects, meaning, for instance, that a given rhythm might favor plasticity in circuits that inhibit, for example, increasing spasticity, or that support recovery. This relation between characteristics of mental activity and differences in cortical plasticity phenomena has been demonstrated in healthy subjects (Pichiorri et al. 2011). Relations between mental activity and "bad plasticity" have been reported in subjects using MI for controlling central pain (Gustin et al. 2008). The possibility of sustaining "bad" plasticity during BCI training has already been advanced but it has generally been discarded as unlikely at least in the classical BCI settings (Schneider et al. 2013). This statement has to be reconsidered when addressing conditions quite different from those present in the "therapy" BCI setting. In this BCI application, brain rhythm is not used to communicate but rather the "therapy" and modification of the related brain circuits is the principal target of the intervention.

4.4 BCI for Rehabilitation of Cognitive and Behavioral Deficits

Besides motor function, cognitive functions such as executive planning, attention, and memory can also be enhanced through modulation of brain rhythms (Serruya and Kahana 2008). Applications have included sustained attention (Egner and Gruzelier 2001, 2004), working memory (Vernon et al. 2003), music (Egner and Gruzelier 2003), dance performance (Raymond et al. 2005a), and mood enhancement (Raymond et al. 2005b). Up to now, BCI neurofeedback applications for cognitive/behavioral rehabilitation have been almost exclusively limited to epilepsy and attention deficit/hyperactivity disorder (ADHD). Epilepsy application suggested that learning to control brain patterns by neurofeedback training might help to reduce the frequency of seizures (Kotchoubey et al. 2001; Strehl et al. 2005). Regarding ADHD, neurofeedback training in addition to behavioral therapeutic approaches has been suggested to improve cognitive and behavioral performances (Strehl et al. 2007).

Besides epilepsy and ADHD, attempts to improve non-motor functions through brain rhythm control also included the treatment of cognitive symptoms following traumatic brain injury (TBI). In particular, data indicate that, at least for attention abilities, EEG-guided biofeedback approaches, either alone or in association with cognitive strategy training, are helpful in sustaining recovery (Thornton and Carmody 2009).

Obviously the same caveat about the possibility of sustaining bad plasticity indicated in the previous section also applies to BCI application to cognitive impairments. Furthermore, BCI application to cognitive and even more to behavioral functions triggers particular ethical aspects. One obvious topic regards the definition of normality and the need to treat within the realm of behavior and cognition. This aspect has been addressed many times and a thoughtful discussion would be beyond the scope of the present topic (Tennison and Moreno 2012; Kadosh et al. 2012; Rachul and Zarzeczny 2012). More specific to BCI therapeutic applications is the idea of a self-sustaining apparatus that in more or less independent closed loops modifies someone's behavior. This setting is quite new and specific to the BCI-neurofeedback approach and potentially harmful. At present data are not sufficient to draw a complete scenario but it is worth considering the quite profound ethical issues related with these applications.

4.5 BCI-Assisted Mental Practice and Rehabilitation

Notwithstanding the numerous novel approaches proposed to boost motor recovery after brain lesions, rehabilitative interventions aimed at motor recovery are still mainly based on active movement training and passive mobilization (Sharma and Cohen 2012). Among the new interventions proposed, motor imagery (MI) represents an intriguing new "backdoor" approach to access the motor system and rehabilitation at all stages of stroke recovery (Liu et al. 2004; Guttman et al. 2012). MI can be defined as a dynamic state during which the representation of a specific motor action is internally rehearsed without any overt motor output, and it is governed by the principles of central and peripheral motor control (Jeannerod and Decety 1995). This is likely the reason why mental practice using MI training results in motor performance improvements (Short et al. 2005). In addition, MI training can independently improve motor performance and produce similar cortical plastic changes (Mulder 2007), thus providing a useful alternative when physical training is not possible. MI training combined with conventional physiotherapy has been reported in one clinical trial with subacute to chronic stroke patients and it demonstrated a greater improvement of hand function with additional mental practice (Hardy et al. 2010). On the other hand, a more recent randomized controlled trial on a cohort of stroke patients showed no efficacy of motor imagery on hand motor recovery with respect to other mental task practice and/or usual treatment (Ietswaart et al. 2011). Clinical trials involving MI have to face specific difficulties mainly related to problems of measuring performance and compliance. When dealing with a pure mental task, despite the instruction provided, it is particularly hard to control for the cognitive strategy employed. For instance, when aiming at activating the motor networks by MI it is crucial to perform the mental task from the first-person perspective (so-called kinesthetic MI), and not from the third-person perspective or with visual imagery that would specifically activate visual networks (Neuper et al. 2006). Furthermore, as stated above, the challenge neurorehabilitators are faced with is clear: Modulating the sensorimotor experience to induce specific forms of plasticity to boost relearning processes. BCI technology is the right approach for controlling for the target circuit of a given rehab intervention when no motor outputs can be used. Thus, within the context of MI training, BCI technology may allow individual MI ability to be objectified and monitored, both in terms of performance (relation between subject's MI performance and subject's level of accuracy in controlling basic BCI applications) and compliance (identification of a correct MI task which is needed to achieve BCI control).

Within the EC-founded research project TOBI (http://www.tobi-project.org) the use of BCI technology has been proposed to overcome the intrinsic limitations of MI training for motor recovery. In particular the BCI approach has been implemented to enhance hand function recovery in stroke patients. In Fig. 4.1 the setup developed for the TOBI BCI prototype to support the MI-based hand treatment of stroke survivors is depicted. Preliminary results of this approach have

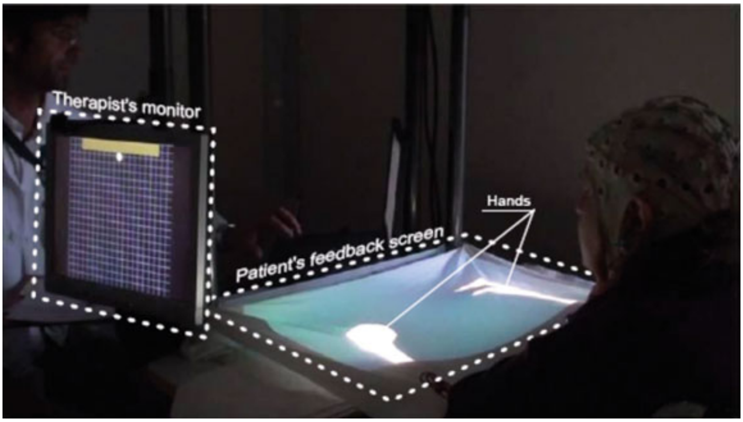

Fig. 4.1 TOBI BCI prototype to support MI-Scalp EEG potentials are collected from 31 positions and data acquisition, online EEG processing, and feedback to the therapist are performed using BCI2000 software. During the session, the patient is seated while hands are covered by a screen. Dedicated software provides a visual representation of the patient's hands, matching the shape, color, and size of the real hand. The "virtual" hand is then projected over the screen matching the position of the real hands positioned under the screen. The therapist has to continuously monitor the patient's mental "activity" by means of the continuous BCI feedback (currently a moving cursor) displayed on a dedicated screen and rewards the patient or corrects his performance. The patient is asked to perform motor imagery of the affected hand and this generates a visual "illusion" of hand movement each time (trial) the patient successfully controls the grasping or the opening of the "fake" hand

recently been published (Mattia et al. 2013; Pichiorri et al. 2012). In extreme synthesis, in the cited approach a mix of BCI and neurofeedback models is employed. The tool is based on a classical BCI system with an external device, producing the movement of a fake hand, that is controlled by brain activity. Notably, in this approach the brain–machine loop is not automatic but is mediated by therapist intervention, allowing adaptation to the patient's capacity and performance monitoring. On the other hand the final objective is not the movement of the fake hand but, as in a neurofeedback protocol, the training of a specific brain rhythm by adding up the effects of MI and visual feedback of the imaged movement. Preliminary results show this approach to be more effective than MI alone in promoting recovery (Mattia et al. 2013).

As stated above, BCI training for rehabilitative application is not limited to the acquisition of a good control of the system; it is also directed toward identification of the brain activity more reliable for sustaining function recovery. In the cited TOBI study this aim has been considered by immersing the patient in a setting which helps him to keep his attention focused on the required task and on the final objective of the training by providing a feedback congruent with the task he is performing.

In this way it is hypothesized that the visual or somatosensory input resulting from the neurofeedback induces plastic changes in the circuits of the central nervous system that are critical for the task. In the absence of more strict characterization of the "correct" brain activity to sustain recovery, the proposed approach is an attempt to guide the BCI training following current knowledge linking mental activity and motor recovery.

4.6 Ethical Issues (Caveats) Emerging from the Therapeutic Use of BCI

In the previous sections we reported on a different use of BCI technology. We now focus on two main ethical issues stemming from this approach – namely thepossibility of iatrogenic effects because of potentiating maladaptive circuits and difficulties in addressing cognitive/behavioral performances in an uncontrolled loop.

4.6.1 Iatrogenic Effects

The proposed BCI-based MI training for motor recovery after stroke is based on repetitive use of stereotyped brain signals within the context of BCI training-induced plasticity. This concept implies that we can guide neuronal rewiring by mental activity. At present very little is known about relations between mental activity and functional recovery. One first obvious statement is that a brain that suffered from a stroke is by no means the same as a healthy brain. The brain activity associated with a given function might therefore be quite different from the physiological one after a stroke. Using BCI approaches to sustain recovery would imply knowing beforehand which will be the right "brain activity" to train to obtain an optimally recovered function. At present we are still missing this piece of information and many variables, such as lesion localization, compensatory strategies, and patient compliance, may influence the characteristics of the optimal brain activity for a given rehabilitation context. The multifactorial framework of influences makes it difficult to predict the brain activity to train in the absence of experience-driven data. Thus it is conceivable that a given "brain activity", although correct in a healthy brain, might not be the right one to sustain recovery. Following this line of thought it could be argued that through BCI it could be possible to sustain a brain activity that inhibits rather than supports recovery. To avoid this possible negative effect, brain algorithms capable of developing patient-tailored BCI training that can adapt or modify itself as long as recovery in ongoing are the right line to pursue for a greater use of BCI-based approaches in neurorehabilitation. To achieve this goal, large libraries of task-related brain rhythms from neurological patients at different stages of recovery are needed. In the absence of such hard data, approaches like that of the TOBI project presented here are needed to guide the choice of the brain rhythm to train, and careful control strategies have to be implemented to reduce the risk of BCI therapy deriving negative effects.

4.6.2 Cognitive/Behavioral Treatments

As often with therapeutic approaches aiming at controlling behavior, special attention to ethical issues is mandatory. This aspect is even more important when supposed "brain reading" techniques such as BCI are involved (Farah 2002). Particularly in the context of neurorehabilitation it should be stressed once more that the "brain reading" approach has to face a damaged brain and that in such a condition the definition of "normality" is even more foggy than usual. While it might seem straightforward to guide the recovery of some cognitive functions like attention or speech, the application of these "objective" approaches to areas like emotion, affection, and aggression is obviously less direct. Although at present no such studies have been attempted, the encouraging results in treating attention and ADHD behavioral disorders with brain activity training would in a short time support proposals of addressing with BCI-derived technologies also disabilities in emotion, affection, or aggression control for instance in traumatic brain injury patients. This ethical aspect is not unique to BCI but is common to other approaches influencing behavior like drugs or surgery or more recently deep or transcranial brain stimulation (Heinrichs 2012). Nevertheless, the idea that an individual can modify his affectivity or aggressiveness by training neural activity and that this can be achieved by the use of a machine that reads someone's thoughts and redirects them might have quite an impact on the general public and in the general perception of this therapy. As recently stated by Allison (2011), the future of BCI research – and we would particularly stress its use in a therapeutic environment – will depend greatly on the correct perception of benefit and risk of its use. To achieve this goal, a shared terminology together with high sensibility to ethical issues are key elements to supporting the exploitation of BCI outside the classical communication and control fields of application.

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